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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,555	02/20/2002	Michael Cappello	OCR-1001.US	2094

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 09/17/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,555	CAPPELLO ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-19* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because non-initialed and/or non-dated alterations have been made to the name and address of inventor, Lisa Harrison. See 37 CFR 1.52(c).

Election/Restrictions

2. Applicant's election of Group I, claims 1-19 in Paper No. 11 is acknowledged. Claim 20 has been cancelled. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Sequence Listing

3. Applicants' amendment regarding sequence listing filed September 9, 2003 is acknowledged, and CRF has been entered.

Informalities

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (page22, line 21). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-6 and 8-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide of SEQ ID NO:2 isolated from Ancyclostoma caninum or cloned, does not reasonably provide enablement for a fragment or variant of SEQ ID NO:2 exhibiting at least 50% sequence homology to the naturally occurring polypeptide and inhibiting platelet function, or a purified polypeptide isolated or cloned from a hookworm having the activity of inhibiting platelet function, where the sequence of the polypeptide is not defined; a composition or a pharmaceutical composition comprising the polypeptide; or a method for treating a patient by administering a hookworm polypeptide, where the disease is not identified. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-6 and 8-19 are directed to a purified polypeptide of SEQ ID NO:2, or a fragment or variant thereof exhibiting at least 50% sequence homology to the naturally occurring polypeptide, wherein the fragment or variant inhibits platelet function (claims 1-6); a purified polypeptide from a hookworm, which inhibits platelet function (claims 12-16); a composition or a pharmaceutical composition comprising the polypeptide (claims 8, 11, 17 and 19); or a method for treating a patient by administering the polypeptide (claims 9 and 18). The specification, however, only discloses cursory conclusions (pages 3-4) without data supporting the findings, which state that a polypeptide is isolated and purified from Ancyclostoma caninum hookworms, and then cloned, this polypeptide (SEQ ID NO:2) inhibits platelet aggregation and adhesion in

response to various agonists by interfering with the binding of at least one cell surface integrin; the invention also provides fragments or variants of the polypeptide exhibiting at least 50% sequence homology to the naturally occurring polypeptide, which exhibit the same biological properties as the native compound; and methods of using these polypeptides in the treatment of diseases. There are no indicia that the present application enables the full scope in view of polypeptides obtained from hookworms and their use in the treatment of diseases as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the presence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the variants or fragments of SEQ ID NO:2, the polypeptide obtained from hookworms, and treating conditions for diseases using the polypeptide, which are not adequately described or demonstrated in the specification.

(2). The presence or absence of working examples:

The specification indicates an extract and an excretory/secretory product (ES) of Ancyclostoma caninum, and a hookworm platelet Inhibitor (HPI), SEQ ID NO: 2 inhibit platelet aggregation and adhesion, especially inhibition of fibrinogen binding to GP IIb/IIIa or inhibition

of collagen binding to GPIa/IIa by HPI (Examples, pages 11 -23). There are no other working examples indicating the claimed variants or methods in association with the claimed invention.

(3). The state of the prior art and relative skill of those in the art:

The prior art (e.g., Pritchard *et al.*, WO 95/12615; Furmidge, Parasitology 112, 81-87 (1995)) teach the excretory/secretory product (ES) products from the human hookworm Necator americanus inhibit the activity of Factor Xa and platelet aggregation. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on identities of variants or fragment s of SEQ ID NO:2, and of hookworm peptides, and the treating conditions for various platelet related diseases using the polypeptide and the effect of the polypeptide to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass many peptide variants, the treating conditions such as the dose of the peptides used and the effects of the peptides in the treatment of diseases are not described in the specification, the invention is highly unpredictable regarding the amino acid sequence of the hookworm peptide and the outcome of the treatment using the hookworm peptide.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to fragments or variants of SEQ ID NO:2 or hookworm polypeptides inhibiting platelet function; a composition or a pharmaceutical composition comprising the hookworm polypeptide; or a method for treating a patient by administering the polypeptide. The specification indicates an extract and an excretory/secretory product (ES) of Ancyclostoma caninum, and a hookworm platelet Inhibitor (HPI), SEQ ID NO: 2 inhibit platelet

aggregation and adhesion (Examples, pages 11 -23), and Examples have indicated one hookworm polypeptide is identified as SEQ ID NO:2. However, the specification has not identified the variants or fragments of SEQ ID NO:2 or other hookworm polypeptides besides SEQ ID NO:2 inhibiting platelet function, nor has demonstrated the use of any hookworm polypeptide in the treatment of diseases. There are no working examples indicating the sequence identities of various hookworm polypeptides other than SEQ ID NO:2 and the treating conditions for various diseases using the hookworm polypeptide. Furthermore, there is no *in vivo* data indicating the hookworm polypeptide is effective in inhibiting platelet function in patient nor demonstrating any disease being treated. Therefore, it is necessary to have additional guidance on the identity of the hookworm polypeptide, and the treating conditions such as dose and time for diseases using the peptide, and to carry out further experimentation to assess the in vivo effect of the hookworm peptides inhibiting platelet function.

(6). Nature of the Invention

The scope of the claims includes many structural variants, however the specification has not demonstrated the use and the effects of these peptide variants in the treatment of diseases. Thus, the disclosure is not enabling for reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed variants, and the teaching in the specification is limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effect of the claimed invention.

6. Claims 1-6 and 8-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-6 and 8-19 are directed to a purified polypeptide of SEQ ID NO:2, or a fragment or variant thereof exhibiting at least 50% sequence homology to the naturally occurring polypeptide, wherein the fragment or variant inhibits platelet function; a purified polypeptide from a hookworm, which inhibits platelet function; a composition or a pharmaceutical composition comprising the polypeptide; or a method for treating a patient by administering the polypeptide. The specification indicates that a polypeptide is isolated and purified from Ancyclostoma caninum hookworms, and then cloned, this polypeptide (SEQ ID NO:2) inhibits platelet aggregation and adhesion in response to various agonists by interfering with the binding of at least one cell surface integrin; fragments or variants of the polypeptide exhibiting at least 50% sequence homology to the naturally occurring polypeptide, which exhibit the same biological properties as the native compound; and methods of using these polypeptides (page 3, line 16-page 4, line 2). However, the specification has not identified a specific variant or fragment of SEQ ID NO:2 exhibiting at least 50% sequence homology to the naturally occurring polypeptide and inhibiting platelet function, or a specific polypeptide isolated or cloned from a hookworm other than SEQ ID NO:2, which inhibits platelet function; nor has demonstrated using the polypeptide to treat a patient. There are no examples indicating variants or fragments of SEQ ID NO:2 exhibiting at least 50% sequence homology to the naturally occurring polypeptide, or polypeptides isolated or cloned from hookworms are functional, and the use of these polypeptides in the treatment of platelet related diseases. Without guidance on structure to function/activity of the peptide and the treating conditions for various diseases using the

polypeptide, one skilled in the art would not know which region or residue of the peptide is essential for function/activity, how to identify a functional peptide, and how to use the peptide in the treatment of diseases. The lack of a structure to function/activity relationship and the lack of representative species for the hookworm polypeptide and its use in the treatment of diseases as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-11, 14-16 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 1-11 are indefinite because of the use of the term "at least about". The term "at least about" renders the claim indefinite, it is not clear whether the fragment or varianat of SEQ ID NO:2 has sequence homology more than 50% as to "at least" or less than 50% as to "about" to the naturally occurring polypeptide. Claims 2-11 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend. Use of the term "about 50% or greater" is suggested.

9. Claim 5 is indefinite because the claim does not further limit claim 2, from which it depends.

10. Claims 9 and 18 are indefinite because the claim does not recite the condition or disease

being treated using the claimed polypeptide.

11. Claims 14-16 are indefinite because of the use of the term "GPIIb/IIIa", "GPIa/IIa" or "ADP". The term "GPIIb/IIIa", "GPIa/IIa" or "ADP" renders the claim indefinite, it is not clear what term "GP" or "ADP" means. A fully spelled out word should be indicated at the first occurrence.

12. Claim 7 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

13. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

Christopher S. F. Low
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September 16, 2003